QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

NCI Thyroid FNA Conference

Management of Benign Thyroid Nodules

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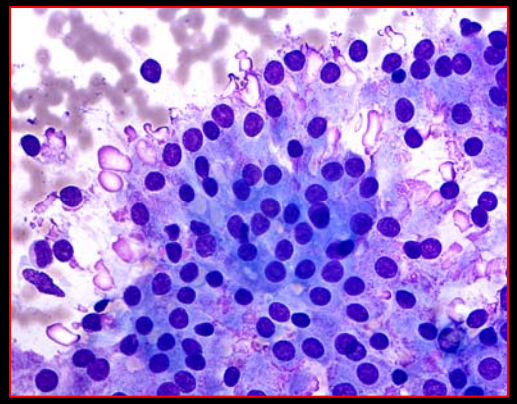

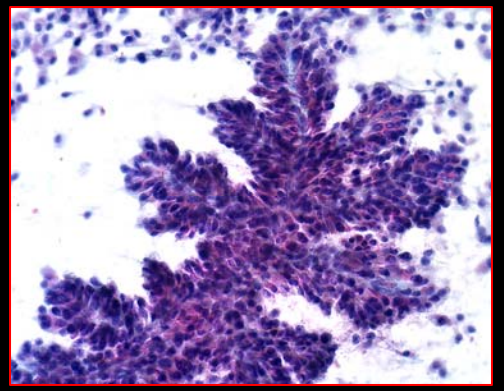

Clinical Issues

- What is the false-negative rate, or did we miss cancer?
- What is the natural history of benign nodule, or do most nodules increase in size?
- Is T4 therapy effective, or does it shrink nodules?
- Is there value in shrinking of removing a benign nodule, or should we leave it alone?

Benign Nodule

Q: How do you follow a patient with a cytologically-benign thyroid nodule?

A. Follow with palpation and, US if indicated, in 12 months
B. Repeat FNA in 6-12 months
C. Use alcohol ablation
D. Thyroxine (T4) therapy
E. No Rx or F-U; dism patient

Follow-Up of Benign Nodules

Wiersinga Wm, 1995

- One might opt for repeat palpation and FNAC 1 year after a benign FNA result

ATA, 2000

- Use US in follow-up (35%)

AACE, 2006

- Follow benign nodules

ATA, 2006

- Easily palpable benign nodules do not require US monitoring, but patient should be followed clinically at 6-18 month intervals

Thyroid FNA Results

	Cases				False-neg rate %	False-pos rate %	Sensi-tivity %	Speci-ficity %
	Total No.	Operated No.	Malignant No.	Malignant %				
Gardiner et al	1,465	207	46	22	11.5	0.0	65	91
Hawkins et al	1,399	415	73	18	2.4	4.6	86	95
Khafagi et al	618	258	44	17	4.1	7.7	87	72
Hall et al	795	72	37	51	1.3	3.0	84	90
Altavilla et al	2,433	257	49	19	6.0	0.0	71	100
Caplan et al	502	185	64	35	9.3	4.0	91	99
Gharib and Goellner	10,971	1,750	682	39	2.0	0.7	98	99
Total	18,183	3,144	995	32	5.2	2.9	83	92

Gharib H and Goellner: Ann Intern Med, 1993

FNA Results

Cytology	Results (%)	Probablility of malignancy (%)
Benign (negative)	65	<1
Malignant (positive)	5	>99
Nondiagnostic (unsatisfactory)	20	<3
Suspicious (indeterminate)	10	20

Gharib H and Papini E: Endocrinol Metab Clin N Am 36:707, 2007

Reaspiration of Cytologically-Benign Nodule is Not Necessary

- 116 pt with benign FNA
- Rebiopsy an all in one

  16 had 3 FNAs
- Repeat FNA

  Identical in 105 (90%)

  Identical after 2 repeat FNA

  Changed colloid to cyst in 11 (9.5%)

Eur J Endo 132:677, 1995

Reaspiration of Cytologically-Benign Nodule is Necessary

- 235 pt with benign FNA
- Followed for average 2.9 yr
- Repeat FNA
  - Benign in 204 (86%)
  - Non-dx in 19 (8%)
  - Suspicious in 11 (5%)
  - Malignant in 1 (0.4%)
- Rebiopsy reduces false-negative rates

Endocr Pract 7:237, 2001

Follow-Up of Enlarging Benign Nodules

AACE, 2006

- Reaspirate enlarging nodules, recurrent cysts, or if no shrinkage after T4 therapy

ATA

- Growing nodules that are benign after reaspiration should be considered for continued monitoring or intervention with surgery; there are no data on the use of T4 in this group

Percutaneous Ethanol Injection (PEI)

- Intranodal injection of 95% alcohol with US guidance
- Effective for benign cysts; 62% require 1 Rx
- Minor side effects
- No longer used for hot nodules or benign, solid nodules

Valcavi R and Frasoldati A: Endor Pract 10:269, 2004

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US-FNA For Everyone?

Use for

- Nonpalpable nodule
- Small (<1 cm) nodule
- Complex lesion
- Lymph node

Castro R and Gharib H: Ann Intern Med 142:926, 2005

Indications for US-FNA

AACE, 2006

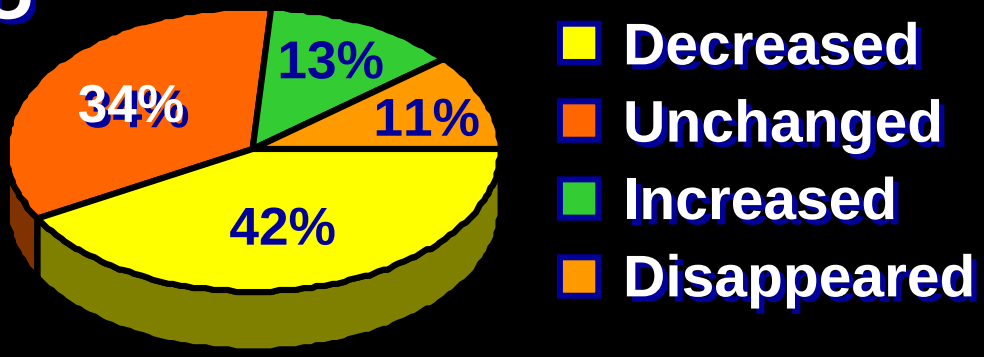
- Any size nodule with Hx of radiation, FMTC or MEN2
- Any size nodule with suspicious US features
- For nodules exhibiting extracapsular growth on cervical nodes
- Impalpable or <1 cm nodule

T4 Suppressive Therapy Why Should It Work?

- Because TSH stimulates and maintains normal thyroid follicular cell function and growth, therefore its suppression should shrink nodules

Nodular Thyroid Disease
Natural History

- 2,609 pt with nodules; 441 surveyed; 140 examined
- F-U 10-30 yr; mean 15±4.5
- By US exam nodules were single (30%) and multiple (68%)
- Nodule status on F-U



Kuma K et al: WJS 18:495, 1994

T4 Suppressive Therapy

- Results in sustained TSH suppression and subclinical hyperthyroidism
- In fact, most common cause of subclinical hyperthyroidism is T4 treatment
- Significant treatment risks include cardiac, bone, and death

T4 Suppressive Therapy Summary

- It is apparent that the therapeutic benefit of L-T4 suppression therapy on benign solitary thyroid nodules is limited to a subset of patients
- Based on controlled studies, we found that 20-23% of patients show clinically significant regression (≥50% reduction in nodule volume) during thyroid hormone suppression therapy

Csako G et al: Medicine 79:9, 2000

T4 Suppressive Therapy

- 9 studies (596 pt)
- Changes in T4 and TSH after T4 indicated good compliance
- Nodule volume decreased significantly in only <20% of treated group
- T4 suppressive therapy led to a nonsignificant improvement in the rate of response to therapy (defined as ≥50% nodule volume reduction by US) (pooled RR 1.83, 95% CI 0.9-3.73)

Richter B et al: Endo Metab Clin N Am 31:699, 2002

Expert Opinion

- “We conclude that there is no certain proof that suppression of nodular thyroid with T4 is beneficial in most patients and its continued use should be discouraged…
- …Nodule shrinkage for its own sake, is a surrogate outcome that may not be of clinical value to patient or physician”

Gharib H and Mazzaferri EL: Ann Intern Med 128:386, 1998

Expert Opinion

Although this treatment has been abandoned in our country (Denmark), it is still the routine choice of nearly half of ATA and ETA members. In view of the potential side effects and the questionable efficacy, it is surprising that 50-70% aim at subnormal TSH levels and treat more than one year.

Hagedus L et al: Endocr Rev 24:102, 2003

Guidelines

AACE, 2006

- Currently, routine T4 therapy in pt with thyroid nodules is not recommended
- Consider T4 therapy for pt in iodine deficiency, young pt with small nodule, nodular goiter without autonomy
- Avoid T4 therapy in most cases especially for large nodules, clinically suspicious lesions, postmenopausal women, pt with cardiac or systemic disease

ATA, 2006

- The panel does not recommend suppression therapy of benign thyroid nodules

Conclusions

- Nodules with benign FNA should be followed by palpation; use of US for small nodules or MNG is endorsed
- Routine reaspiration is not recommended; repeat FNA if nodule increases is size
- PEI is effective for benign thyroid cysts
- T4 therapy to suppress TSH and shrink thyroid nodule is not recommended
- Thyroid FNA false-negative rates should be <2%